or in view of WO 97/25303 ("Ryan"). These rejections are respectfully traversed. Claims 1, 3, and 8-11 have been modified. Support is at least found in the specification at page 11, line 20 and Example 3. Claims 1-11 remain pending.

Priority Document

It is believed that applicant does not need to submit a certified copy of the priority document because M.P.E.P. § 1893.03(c) states that the copy of the priority document provided by the International Bureau satisfies the submission requirement.

Rejection under 35 U.S.C. § 103(a)

Claims 1-11 were rejected under 103(a) as being unpatentable over Kawai alone or in view of Ryan. The Examiner acknowledged that Kawai "fail[s] to teach the amount of HFIP [unreacted 1,1,1,3,3,3-hexafluoroisopropyl alcohol] present in the crude sevoflurane [fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether]" at page 3 of the Office Action.

In view of this admission, fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether (or crude sevoflurane) was produced 110 times (Runs 1 through 110) in accordance with Examples 1 and 6 of Kawai, to determine the amount of the unreacted 1,1,1,3,3,3-hexafluoroisopropyl alcohol ("HFIP") present in the crude sevoflurane of Kawai. See Experiment 1 of the attached Declaration Under 37 C.F.R. 1.132 ("Declaration"). The sevofluranes produced in Runs 1-110 were found by gas chromatography to contain HFIP in amounts shown in the Declaration. See Declaration at 4-6. The HFIP contents of sevofluranes of Runs 1-110 have a relatively small variation or deviation and had an average of 4.71 wt% HFIP. See Declaration at 6.

According to Experiment 2, as set forth in the Declaration, the sevoflurane obtained in Run 1 (containing 4.91 wt% of HFIP) was washed with 4% sodium hydroxide aqueous solution in accordance with Example 6 of Kawai. It was found

that the HFIP content of sevoflurane of Run 1 was reduced from 4.91 wt% to 0.05 wt% by this alkali washing. In other words, the HFIP content after the alkali washing was reduced to only about 1/100 of that before the alkali washing.

In contrast, Example 3 of instant specification establishes that the HFIP content of fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether or sevoflurane is reduced by the alkali washing from 0.25 wt% to an amount less than a detection limit of 1 ppm (i.e., 0.0001 wt%). Thus, the HFIP content after the alkali washing of the claimed process is unexpectedly less than 4/10,000 of that before the alkali washing. Therefore, the amount of the reduction of the HFIP content by the alkali washing is unexpectedly much greater in the case in which the HFIP content of the fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether before the alkali washing is 0.25 wt% as in Example 3 of instant specification, as compared with the case in which the HFIP content of the crude sevoflurane before the alkali washing was 4.91 wt%. See Experiments 1-2 of the Declaration and Example 6 of Kawai.

According to the results of Experiments 1-2 of the Declaration, it is understood that the HFIP content of fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether was reduced by alkali washing from 10 wt% to only 0.1 wt% (i.e., a decrease to 1/100) in Example 1 of the specification, from 10 wt% to only 0.8 wt% (i.e., a decrease to 8/100) in Example 2 of the specification, and from 5 wt% to only 0.05 wt% (i.e. a decrease to 1/100) in Comparative Example 3 of the specification, as compared with the above-mentioned unexpected result (a decrease to less than 4/10,000) of Example 3 of instant specification where the concentration of HFIP is not greater than about 0.25% by weight. In other words, Examples 1 and 2 and Comparative Example 3 of the specification are outside the scope of amended claim 1. Thus, the claimed invention as amended and as supported by Example 3 of the specification is unobvious over Comparative Example 3 of the specification in contrast to the Examiner's assertion at lines 1-6 of page 5 of the Office Action.

Thus, the amount of HFIP in crude fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether is critical in obtaining fluoromethyl 1,1,1,3,3,3-

hexafluoroisopropyl ether of high purity and the effect of the claimed processes in removing unreacted HFIP depends on the initial concentration of unreacted HFIP as recited in independent claims 1, 8, 9, 10, and 11.

Furthermore, it is clear from Example 3 of instant specification that a HFIP content less than a detection limit of 1 ppm may be obtained by the claimed process if the initial HFIP content of the crude sevoflurane is not greater than about 0.25 wt%. In other words, the inventors unexpectedly found that it is necessary to adjust the initial HFIP content of the crude sevoflurane to 0.25 wt% or less before conducting the alkali washing, for the purpose of obtaining sevoflurane of high purity. Therefore, the claimed recitation of not greater than about 0.25 wt% by weight produces an unexpected result (i.e., the obtainment of high purity fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether).

The criticality of the lower limit (i.e., 1) of the claimed range of the chemical equivalent ratio of the basic substance to HFIP is supported by the results of the Declaration. According to Experiment 3 of the Declaration, the HFIP content of fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether was reduced by the alkali washing from 0.25 wt% to an amount less than a detection limit of 1 ppm (i.e., a decrease to less than 4/10,000) where the equivalent ratio of sodium hydroxide to HFIP was reduced from 1.2 (Specification Experiment 3) to 1 (Declaration Experiment 3). In other words, it is possible to obtain the above-mentioned unexpected beneficial result (as shown in Declaration Experiment 3) by the claimed invention, even when the claimed chemical equivalent ratio is at the lower limit of the claimed range (i.e., not less than 1).

The Ryan reference does not cure the deficiencies of Kawai. Accordingly, withdrawal of the rejection of claims 1-11 is respectfully requested.

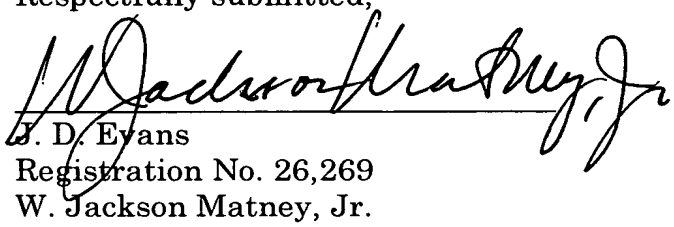
In view of the foregoing amendments and remarks, the application is respectfully submitted to be in condition for allowance, and prompt favorable action thereon is earnestly solicited.

If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response; please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket #3007/48236).

Respectfully submitted,

September 26, 2002



J. D. Evans
Registration No. 26,269
W. Jackson Matney, Jr.
Registration No. 39,292

CROWELL & MORING LLP
P.O. Box 14300
Washington, DC 20044-4300
Telephone No.: (202) 624-2500
Facsimile No.: (202) 628-8844

MARKED-UP VERSION TO SHOW CHANGES

IN THE CLAIMS

1. (amended) A process for purifying fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether, comprising:

causing fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether containing [less] not greater than about [1] 0.25% by weight of at least 1,1,1,3,3,3-hexafluoroisopropyl alcohol, to contact with a basic aqueous solution which contains a basic substance in an amount providing a chemical equivalent ratio of said basic substance to 1,1,1,3,3,3-hexafluoroisopropyl alcohol being within a range of not less than 1 so as to [obtain] remove the 1,1,1,3,3,3-hexafluoroisopropyl alcohol from the fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether [which substantially does not contain 1,1,1,3,3,3-hexafluoroisopropyl alcohol].

3. (amended) A process as claimed in Claim 1, wherein the causing [step] is carried out at a temperature ranging from 0 to 60°C.

8. (amended) A process for purifying fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether, comprising:

providing fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether containing [less] not greater than about [1] 0.25% by weight of at least 1,1,1,3,3,3-hexafluoroisopropyl alcohol, and a basic aqueous solution which contains a basic substance in an amount providing a chemical equivalent ratio of said basic substance to 1,1,1,3,3,3-hexafluoroisopropyl alcohol being within a range of not less than 1; and

causing said fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether containing 1,1,1,3,3,3-hexafluoroisopropyl alcohol, to contact with said basic aqueous solution containing said basic substance so as to [obtain] remove the 1,1,1,3,3,3-

hexafluoroisopropyl alcohol from the fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether [which substantially does not contain 1,1,1,3,3,3-hexafluoroisopropyl alcohol].

9. (amended) A process for purifying fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether, comprising:

providing fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether containing [less] not greater than about [1] 0.25% by weight of at least 1,1,1,3,3,3-hexafluoroisopropyl alcohol, and a basic aqueous solution which contains a basic substance in an amount providing a chemical equivalent ratio of the basic substance to 1,1,1,3,3,3-hexafluoroisopropyl alcohol being within a range of not less than 1;

forming a reaction system in which inorganic acid radical is substantially absent; and

causing said fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether containing 1,1,1,3,3,3-hexafluoroisopropyl alcohol, to contact with said basic aqueous solution containing said basic substance so as to [obtain] remove the 1,1,1,3,3,3-heafluoroisopropyl alcohol from the fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether [which substantially does not contain 1,1,1,3,3,3-hexafluoroisopropyl alcohol].

10. (amended) A process for purifying fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether, comprising:

causing fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether containing [less] not greater than about [1] 0.25% by weight of at least 1,1,1,3,3,3-hexafluoroisopropyl alcohol, to contact with basic aqueous solution containing a basic substance, in a reaction system in which inorganic acid radial is substantially absent so as to [obtain] remove the 1,1,1,3,3,3-hexafluoroisopropyl alcohol from the fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether [which substantially does not contain 1,1,1,3,3,3-hexafluoroisopropyl alcohol].

11. (amended) A process for purifying fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether, comprising:

forming a reaction system in which inorganic acid radial is substantially absent; and

causing fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether containing [less] not greater than about [1] 0.25% by weight of at least 1,1,1,3,3,3-hexafluoroisopropyl alcohol, to contact with a basic aqueous solution containing a basic substance, in said reaction system so as to [obtain] remove the 1,1,1,3,3,3-hexafluoroisopropyl alcohol from the fluoromethyl 1,1,1,3,3,3-hexafluoroisopropyl ether [which substantially does not contain 1,1,1,3,3,3-hexafluoroisopropyl alcohol].